UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,365	04/13/2004	Gavril Pasternak	62069DIV2(51590)	4859

21874 7590 02/18/2010

EDWARDS ANGELL PALMER & DODGE LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
MCMILLIAN, KARA RENITA	
ART UNIT	PAPER NUMBER
1627	
MAIL DATE	DELIVERY MODE
02/18/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/823,365	**Applicant(s)** PASTERNAK ET AL.	
	Examiner KARA R. MCMILLIAN	**Art Unit** 1627	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 21 January 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1627

/Kara R. McMillian/
Examiner, Art Unit 1627

Continuation of 11. does NOT place the application in condition for allowance because: Applicants arguments submitted on January 21, 2010 have been considered but were found not persuasive. Applicants argue that the combination of Elkhoury in view of Elden does not render obvious a synergistically effective composition as two topically administered drugs acting synergistically could not have been expected at the time the instant invention was made. This argument is found not persuasive since as previously argued applicants claims are directed to a method of providing topical analgesia comprising administering synergistically effective amounts of morphine and butamben. Elkhoury et al. and Elden teach overlapping ranges of concentrations of morphine and butamben as claimed in claims 16, 17, 19, 20 and 22-25 of the instant application. One of ordinary skill in the art would also be motivated to combine the morphine and butamben in a composition based on the concentrations taught in the prior art references (0.07% of morphine (Elkhoury et al.) and between 0.2%-20% of butamben (Elden)). Thus it would be obvious to a person of ordinary skill in the art to combine morphine and butamben in the concentrations as taught by Elkhoury et al. and Elden which are the same concentrations as claimed in the instant application. Thus the combination of Elkhoury et al. and Elden renders obvious the administration of a combination of synergistically effective amounts of morphine and butamben for providing topical analgesia since each reference individually teach application of a synergistically effective amount of morphine and a synergistically effective amount of butamben. Applicants argue that the office action discusses post published art (Kolesnikov et al.) and concludes that the synergistic effects of topical lidocaine and morphine were not unexpected. However, Kolesnikov et al. was only discussed since it was introduced by Applicants in the declaration filed on May 1, 2006 by Yuri Kolesnikov and Gavril Pasternak. Kolesnikov et al. was only addressed in response to Applicant's declaration and was not intended to apply as prior art or any basis for rejection. As previously explained, since Applicants introduced Kolesnikov et al. it was pointed out that Kolesnikov et al. conclude that the synergistic effects of topical lidocaine and morphine were not unexpected and that synergistic interactions are more likely when drugs act on different mechanisms, as shown between morphine and butamben (see page 1107). Thus there is a reasonable expectation of success that when butamben is administered topically with morphine, a synergistic effect would occur and therefore the synergistic results as claimed in the instant application is not unexpected. For reasons of record and for the reasons presented above, the previous rejections of the final office action dated October 21, 2009 are hereby maintained.